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A NEW SYNTHESIS

OF

a—ETHYLTRICARBALLYLIC ACID

BY

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CXLII.—*A New Synthesis of α-Ethyltricarballylic Acid.*

By Hooper Albert Dickinson Jowett.

In the preceding paper, it was shown that by the fusion of homopilopic acid with potassium hydroxide an acid of the formula $C_8H_{12}O_6$ was formed and that the properties of this acid corresponded with those of α-ethyltricarballylic acid. As, however, two different melting points have been assigned to this acid and as no derivatives have been described other than the silver salt, it was necessary to prepare the substance and to examine it more fully, so as to be able to identify completely the acid formed from homopilopic acid with the synthetical compound.

α-Ethyltricarballylic acid was first prepared by Auwers (*Ber.*, 1891, 24, 307, 2897) by the condensation of ethyl ethylsodiomalonate with ethyl fumarate and subsequent hydrolysis. The acid, after recrystalsation, melted at 147—148° and was readily soluble in water, but only moderately so in ether; on evaporation, the ethereal solution left an oil which became crystalline. The substance was prepared more recently by Michael (*Ber.*, 1900, 33, 3745) by the same method, but he found that after further purification it melted at 155—157°.

In order to prepare the acid for the purpose of comparison, it was deemed advisable to accomplish the synthesis by an entirely different method, as this at the same time would afford additional proof of the correctness of the constitution of the synthetical acid prepared by Auwers.

Ethyl α-cyano-β-ethylsuccinate was prepared by the general method of preparation of the alkyl-substituted succinic acids described by Bone and Sprankling (Trans., 1899, 75, 839), by condensing the sodium compound of ethyl cyanoacetate with ethyl α-bromobutyrate.

The sodium compound of ethyl α-cyano-β-ethylsuccinate was then condensed with ethyl bromoacetate with the formation of ethyl β-cyano-α-ethyltricarballylate. This stage of the synthesis may be presented by the following equation:

$$CH_2Br{\cdot}CO_2Et + CO_2Et{\cdot}CNa(CN){\cdot}CH(C_2H_5){\cdot}CO_2Et = \\ CO_2Et{\cdot}CH_2{\cdot}C(CN)(CO_2Et){\cdot}CH(C_2H_5){\cdot}CO_2Et + NaBr.$$

The ethyl cyanoethyltricarballylate, on hydrolysis, yielded an acid from which carbon dioxide was eliminated by heating at 180° with the formation of α-ethylcarballylic acid.

These condensations took place readily, the yield of cyano-esters in the first and second stages of the synthesis being 50 and 70 per cent. respectively of the calculated amounts. As these cyano-esters have not been previously prepared, their boiling points and densities were determined.

α-Ethyltricarballylic acid as thus prepared was found to agree in its general properties with those previously recorded, and after recrystallisation melted at 157° (corr.), thus confirming the figure given by Michael. Of its derivatives described later, the calcium salt is very characteristic; it is fairly soluble in cold water, but on warming the aqueous solution, the liquid is converted into a solid jelly, which liquefies on cooling. This gelatinisation of the calcium salt, coupled with the melting point of the acid, affords the best means of identifying the substance.

EXPERIMENTAL.

Ethyl α-Cyano-β-ethylsuccinate, $CO_2Et \cdot CH(CN) \cdot CH(C_2H_5) \cdot CO_2Et$.

This ester was prepared as follows:—28·5 grams of ethyl cyanoacetate were mixed with a solution of 5·75 grams of sodium in 70 grams of absolute alcohol, and to the resulting thick paste 48·75 grams of ethyl α-bromobutyrate were added. The mixture, which became warm, was heated on a water-bath until neutral, which generally required 2—3 hours; it was then cooled, poured into water, and the oil which separated was extracted with ether. The ethereal solution was washed with water, dried over calcium chloride, and then distilled. The residual oil was fractionated under 20 mm. pressure, when a quantity of unchanged ethyl cyanoacetate and ethyl α-bromobutyrate distilled below 100°, but the greater portion of the liquid distilled at 160—170°, leaving only a very small residue in the flask. On refractionation, the portion distilling at 160—170° was collected. Of this a portion boiling constantly at 167—168° was set aside for analysis; it had a density d 15°/15° = 1·0647. The yield of product boiling at 160—170° under 20 mm. pressure was 50 per cent. of the theoretical. On analysis:

0·1338 gave 0·285 CO_2 and 0·0916 H_2O. C = 58·1; H = 7·6.
0·1512 ,, 9·4 c.c. nitrogen at 24° and 764 mm. N = 6·8.
$C_{11}H_{17}O_4N$ requires C = 58·1; H = 7·5; N = 6·2 per cent.

The correctness of the formula ascribed to the cyano-ester was proved by the fact that on hydrolysis the compound furnished ethylsuccinic acid melting at 98°, which on analysis yielded the following result:

0·132 gave 0·2372 CO_2 and 0·086 H_2O. C = 49·0; H = 7·2.
$C_6H_{10}O_4$ requires C = 49·3; H = 6·9 per cent.

The characteristic calcium ethylsuccinate was also prepared.

Ethyl β-Cyano-α-ethyltricarballylate,
$CO_2Et \cdot CH(C_2H_5) \cdot C(CN)(CO_2Et) \cdot CH_2 \cdot CO_2Et$.

This cyano-ester was prepared as follows:—To 6 grams of sodium dissolved in 60 grams of absolute alcohol, 45·4 grams of ethyl-α-cyano-β-ethylsuccinate were added. The mixture became warm and very viscid, but no solid separated; after cooling, 33·4 grams of ethyl bromoacetate were added, when a reaction at once took place with evolution of heat and separation of sodium bromide. The mixture was heated for half-an-hour on a water-bath, cooled, and then poured into water. The oil which separated was extracted with ether, the ethereal solution washed with water, dried with calcium chloride, and distilled. The residual oil was carefully fractionated under 20 mm. pressure. Scarcely any liquid distilled below 195°, the greater portion came over between 195° and 215°, leaving a small residue in the flask. On refractionation, the portion distilling at 205—208° under 17—21 mm. pressure was collected, the greater portion, boiling constantly at 208° under 21 mm. pressure, being put aside for analysis and for the determination of its density. The yield of refractionated product was 70 per cent. of the theoretical. On analysis:

0·1716 gave 0·3602 CO_2 and 0·1144 H_2O. C = 57·3; H = 7·4.
0·1756 „ 7·5 c.c. nitrogen at 24° and 764 mm. N = 4·7.
$C_{15}H_{23}O_6N$ requires C = 57·5; H = 7·3; N = 4·5 per cent.

The density at 16° compared with water at 16° was 1·0972.

a-Ethyltricarballylic Acid, $CO_2H·CH(C_2H_5)·CH(CO_2H)·CH_2·CO_2H$.

This acid was obtained from the ethyl cyanoethyltricarballylate in the following manner. The ester was first boiled with five times its weight of 40 per cent. aqueous sulphuric acid in a reflux apparatus until all the oily drops had disappeared, which generally required a period of 24—48 hours. The acid liquid was then saturated with ammonium sulphate and extracted with ether six times. The ethereal extract was distilled to a convenient bulk and extracted with dilute sodium carbonate solution. This was acidified with sulphuric acid, saturated with ammonium sulphate, and extracted with ether. The ethereal solution was washed with water, dried with calcium chloride, distilled to a low bulk, and then poured into ten times its volume of benzene. On standing, crystals separated which were filtered off; these, when dried, melted at 117° with effervescence. The acid was then heated in a small flask in a paraffin bath at 180° until all evolution of gas had ceased. After cooling, the mass was dissolved in a little hot water, boiled with animal charcoal, and filtered. On standing and stirring with a glass rod, the solution became pasty. The crystals were drained on a porous tile and recrystallised from a little water until of constant melting point; thus purified, they melted at 156—157° (corr.). The pure acid required about 20 times its weight of ether to dissolve it, but on evaporating this solution at the ordinary temperature, no crystals separated until all the ether had evaporated, when an oil was left which gradually became solid. On analysis:

0·1974 gave 0·341 CO_2 and 0·106 H_2O. C = 47·1; H = 6·0.
0·198 „ 0·342 CO_2 „ 0·1064 H_2O. C = 47·1; H = 6·0.
$C_8H_{12}O_6$ requires C = 47·1; H = 5·9 per cent.

The *anhydro-acid* was prepared by adding the acid to three times its weight of acetyl chloride and boiling for 2 hours in a reflux apparatus. The acid slowly dissolved and the excess of acetyl chloride was removed by evaporation on the water-bath and subsequent standing in a vacuous desiccator over solid potassium hydroxide. In this way, a hard, sticky varnish was obtained, which could not be crystallised. On analysis:

0·2218 gave 0·4146 CO_2 and 0·1108 H_2O. C = 51·0; H = 5·5.
$C_8H_{10}O_5$ requires C = 51·6; H = 5·4 per cent.

The anhydro-acid dissolved in benzene; on the addition of aniline to the solution, heat was developed, the liquid immediately became cloudy, and an amorphous precipitate separated which, however, could not be obtained crystalline.

The *barium* salt was prepared by digesting an aqueous solution of the acid with excess of barium carbonate until neutral, and filtering. On warming the filtrate, crystals appeared which, however, redissolved on cooling. The filtrate was evaporated to a small bulk, filtered while hot, and the crystals dried, first on a porous tile and finally between blotting paper. Analysis showed that the air-dried crystals contained 7 mols. of water of crystallisation, of which six are removed by heating at 180°:

0·3156 at 180° lost 0·036 H_2O and gave 0·234 $BaSO_4$. H_2O = 11·4; Ba = 43·6.
0·1716 gave on combustion 0·0526 H_2O. H = 3·4.
$(C_8H_9O_6)_2Ba_3,7H_2O$ requires H_2O = 13·4; Ba = 43·8; H = 3·4 per cent.

The *calcium* salt was prepared by digesting an aqueous solution of the acid with excess of calcium carbonate and filtering. The filtrate had the remarkable property of becoming a firm jelly when heated to 100°, and liquefying on cooling. The liquid was evaporated to a small bulk in a vacuum and the calcium salt precipitated with alcohol in a microcrystalline form. On analysis:

0·1886 at 150° lost 0·044 H_2O and on ignition gave 0·0454 CaO. H_2O = 23·3; Ca = 17·2.
$(C_8H_9O_6)_2Ca_3,9H_2O$ requires H_2O = 23·7; Ca = 17·5 per cent.

The *copper* salt, prepared by adding copper acetate solution to an aqueous solution of the ammonium salt of the acid and boiling, was a greenish-blue, flocculent precipitate. On analysis:

0·1972 at 150° lost 0·0272 H_2O and on ignition gave 0·0696 CuO H_2O = 13·8; Cu = 28·2.
$(C_8H_9O_6)_2Cu_3,5H_2O$ requires H_2O = 13·2; Cu = 28·0 per cent.

The *triethyl ester*, prepared in the usual manner by the action of sulphuric acid and ethyl alcohol on the acid, was a limpid, colourless liquid boiling at 170—175° under 16 mm. pressure. On analysis, it furnished the following results:

0·2136 gave 0·457 CO_2 and 0·1574 H_2O. C = 58·3 ; H = 8·2.

$C_{14}H_{24}O_6$ requires C = 58·3 ; H = 8·3 per cent.

An attempt to prepare the amide by mixing the ester with excess of strong ammonia was unsuccessful.

Addendum.—Since this paper was in type the author has received a communication from Dr. Bone pointing out the following passage in a paper, "Researches on the Alkyl Substituted Succinic Acids," by Bone and Sprankling (Trans., 1899, **75**, 864): "Finally, we are studying the interaction of the sodium derivative of ethylic cyanosuccinates and the ethylic salts of α-bromo-fatty acids."

As the purpose for which reference was made to the paper in question only necessitated the reading of that portion of it relating to the details of preparation of the analogous ethyl cyanomethylsuccinate, the concluding paragraph containing the passage referred to most unfortunately escaped my attention.

The necessity for the preparation of α-ethyltricarballylic acid and certain of its derivatives was due to the great importance of identifying beyond question the acid formed by the fusion of homopilopic acid with potassium hydroxide.

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